STRUCTURAL FEATURES OF CLEAVAGE OF NONSYMMETRICALLY SUBSTITUTED 1,3-DIOXOLANES BY THE GRIGNARD REAGENT

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In our plan for the systematic investigation of reactions between 1,3-dioxocyclanes and organomagnesium compounds [1-7], we assigned fundamental importance to the question of structural orientation in cleavage of the nonsymmetrically substituted 1,3-dioxolane ring, for this question is closely linked to the explanation of the reaction mechanism. During interaction of 4-alkyl- and 2,4-dialkyl-1,3-dioxolanes with the Grignard reagent, we would expect the formation of two structurally isomeric hydroxy ethers differing only by the position of the hydroxyl group at the first or the second carbon atom.



However, gas-liquid chromatographic analysis (GLCH) of the reaction products of dioxolanes (I)-(III) with ethylmagnesium bromide revealed the close to exclusive presence of one of the ethers only, and the amount of the second isomer was no more than 4.2% of that of the first (Fig. 1, 2b, and 3b). A first choice between the two possible isomeric structures of (IV)-(VI) and (VII) would be possible on the basis of GLCH, since under chromatographic conditions of the reaction mixture secondary alcohols and branched ethers have a shorter life than the corresponding normally structured isomers; we deduced from the chromatogram (Fig. 1, 2b, and 3b) that 2-oxy-1-methylethyl ethers (IV)-(VI) are mainly formed during the reaction, and these ethers contain the primary hydroxyl group. A small peak found in all three chromatograms preceding the main peak was assigned to isomeric 2-hydroxypropyl ethers (VII) having a secondary hydroxyl. This conclusion was confirmed after careful analysis of IR spectra (Fig. 4) of the purified hydroxy ethers (IV)-(VI) and the chlorides (VIII) and (IX) obtained by substituting the hydroxyl group in the compounds under study by chlorine supplied as thionyl chloride.

(V), (VI) $\xrightarrow{\text{SOCI}_3} \mathbb{R}(C_2H_3)CH = O = CH(CH_3)CH_2CI$ (VIII), (IX) $R = CH_3$ (VIII); C₃H₇ (IX)

For a comparison of IR spectra of hydroxyl ethers known to contain the corresponding primary and secondary hydroxyl group and the β , β -dichlorodiethyl ether (chlorex) (XII), used as standard for the reliable determination of frequencies in chloride spectra (VIII) and (IX), we synthesized the standard hydroxyl ethers $C_{2H_5}CH(CH_3)OCH_2CH_2OH$ (X) and $(C_{2H_5})_2C(CH_3)OCH(CH_3)CH(CH_3)OH$ (XI) by reacting 2-methyl and 2,4,5-trimethyl-2-ethyl-1,3-dioxolanes with ethylmagnesium bromide (yields 84.6 and 82.3% respectively). The IR spectra of the ethers under study and of the standards (X) and (XI) (we used 0.01 M solutions in CCl₄) showed narrow intensive bands in the 3600 cm⁻¹ range, at 3591 (IV), 3589 (V), 3598 (X) and 3578 cm⁻¹ (XI) (see Fig. 4) characteristic for valence vibrations of the hydroxyl participating in the formation of the intra-molecular hydrogen bond in β -hydroxy ethers [8-11]. In full agreement with literature data, the band corre-

Irkutsk Institute of Organic Chemistry, Siberian Division of the Academy of Sciences of the USSR. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 12, pp. 2727-2733, December, 1967. Original article submitted March 13, 1967.



Fig. 1. Chromatogram of products obtained by reaction of 4-methyl-1,3-dioxolane with ethylmagnesium bromide: 1) 1-(2'-oxypropoxy)propane; 2) 1-(1'-methyl-2'-oxyethoxy)propane (IV).

Fig. 2. Chromatogram of the starter 2,4-dimethyl-1,3-dioxolane (a) and its reaction products with ethylmagnesium bromide (b). 1) cis-2,4-Dimethyl-1,3-dioxolane; 2) trans-2,4-dimethyl-1,3-dioxo-lane; 3) not identified; 4) 2-(2'-oxypropoxy)butane; 5) 2-(1'-methyl-2'-oxyethoxy)butane (V).

Fig. 3. Chromatograms of the starter 2-propyl-4-methyl-1,3-dioxolane (a) and products of its reaction with ethylmagnesium bromide (b). 1) cis-2-Propyl-4-methyl-1,3-dioxolane; 2) trans-2-propyl-4-methyl-1,3-dioxolane; 3,4) not identified; 5) 3-(2'-oxypropoxy)hexane; 6) 3-(1'methyl-2'-oxyethoxy)hexane (VI).

sponding to the nonbonded hydroxyl (transconformer) appeared as a shoulder at 3638 (IV), 3636 (V) and 3638 cm⁻¹ (X), the standard hydroxy ether with the primary hydroxyl group, and 3618 cm⁻¹ (XI) which is the standard with the secondary hydroxyl group.

In accordance with literature data, absorption of the monomer hydroxyl in the primary alcohol is seen at 3640 cm⁻¹ [13] while secondary alcohols show a shift of the maximum by about 10 cm⁻¹ toward the lower frequency range and appear at 3622 cm⁻¹ (KP spectrum [12] or at 3630 cm⁻¹ [13]). Tertiary alcohols show absorption in a still lower frequency range: 3615 cm^{-1} (KP spectrum [12], 3620 cm^{-1} [13]). A comparative analysis in the 3600 cm⁻¹ range (see Fig. 4, curves 1-4) points to the presence of a fragment of primary alcohol in the compounds (IV)-(VI) under study.

The same conclusion may be drawn from an analysis of the IR spectra of ethers (IV)-(VI) and (VIII)-(XI) in the C-O valence vibration range (1000-1200 cm⁻¹). Primary and secondary alcohols may be differentiated according to their IR spectra in the range [13-15]. Primary alcohol absorption is seen at approximately 1050 cm⁻¹, secondary at 1100 cm⁻¹; absorption bands are inconstant and depend on the overall molecular structure; thus an additional α branching will lead to a frequency decrease by about 15 cm⁻¹. A comparison of hydroxy spectra with those of the corresponding chlorides whose absorption in this range is determined only by the ether fragment leads to isolation of a band corresponding to the hydroxyl. For the hydroxy ethers (IV) and (V), this appears at 1051 and 1054 cm⁻¹ (Fig. 4, curves 3 and 4), in agreement with literature data [13, 14], and shows the presence of the primary hydroxyl. In this range, the spectra of the ethers (IV) and (V) are also very close to the spectrum (curve 2) of the standard (XI) (secondary hydroxyl) where the sharp maximum around 1050-1060 cm⁻¹ is absent. As was to be expected, the band observed for ethers (IV) and (V) has shifted by about 10 cm⁻¹ toward lower frequencies, compared to the analogous band in the spectrum (X) (1066 cm⁻¹); this is due to α branching.

Besides, another band is found at 745 cm⁻¹ in the IR spectra of the chlorides (VIII) and (IX) (curves 5, 6) in the C--Cl valence vibration range; this band refers to the transconformer [16]. The band at 670 cm⁻¹ (curve 5) corresponds to the Hoesch conformation. The same bands are also seen in the chlorex spectrum (curve 7) and in 2-chloroethylvinyl ether (spectrum not shown), compounds known to contain the chlorine atom in the first carbon at the β position to the ether group. It is also known that vibration of the C--Cl bond in the second carbon radical appears at 615 cm⁻¹ [17].

Based on our findings in the series under study, we may assume to have proven that the Grignard reagent will split 4-alkyl- and 2,4-dialkyl-1,3-dioxolanes almost exclusively at the O_1-C_2 bond. This con-



Fig. 4. IR spectra of hydroxy- and chloro ethers. 1) (XI); 2) (X); 3) (V); 4) (IV); * 5) (VIII); 6) (IX); 7) 2,2'-di-chlorodiethyl ether. Microlayer, spectrometer UR-10. A 0.01 M solution in CCl₄ was used in the 3600 cm⁻¹ range (spectra 1-4).

*The IR spectra of ether (VI) coincide with those of ethers (IV) and (V). clusion may be unexpected at first sight, since the reaction certainly started with coordination of the magnesium compound at location of the free electron pairs of the oxygen [6, 7], and it would appear that in this case the atom O_3 , linked to two secondary radicals should be an important participant in coordination, due to its higher electron density. Thus we would expect the main split at the C_2-O_3 bond, contrary to what happens. However, if the transitory state of the reaction is sufficiently complex and ordered, atom O_3 participation may encounter difficulties of a steric nature.

It may be seen from the chromatograms (see Figs. 2, 3, curves a) that the starter 2,4-dimethyl-1,3-dioxolane (II) and 2-propyl-4-methyl-1,3-dioxolane (III) are mixtures of cis- and trans-isomers in a ratio of 2.01:1.00 and 1.45:1.00 respectively. After the reaction, these ratios change to 1.09:1.00 and 1.16:1.00, i.e., the isomers are split at different rates by the Grignard reagent: kcis/ktrans = 1.25 for (II) and kcis/ktrans = 1.05 for (III) (calculated from the chromatograms).

Peaks 1 and 2 (see Figs. 2, 3) were related to certain configurations of 2,4-dialkyl substituted 1,3-dioxolanes by comparing the boiling points known for each of the 2,4-dimethyl-1,3-dioxolane isomers [18], while isomer volumes were retained under chromatographic conditions providing for fractional isolation of the products according to their bp (squalane for the stationary phase and chromosorb W as carrier). Under these conditions the order of peak size in 1 and 2 was the same as in Figs. 2a and 3a. According to [18], the low-boiling isomer (II) has the cis-configuration, and thus peak 1 was considered to refer to the cis-isomer.

The difference in reactability to the Grignard reagent between cis- and trans-isomers of 2,4-dialkyl-1,3-dioxolanes confirms the assumption on the important role of the space factor at the stage determining the reaction rate. The reason for the structural features of the cleavage may be sought in the lesser spatial penetrability of the C_2-O_3 bond, compared to O_1-C_2 , since the former is screened by the alkyl substituents. Based on experimental data, we proposed earlier [6, 7] the following mechanism for the reaction under study.



Coordination between the oxygen atoms and $MgBr_2$ is unequivocally shown at the first reaction stage by the practically quantitative precipitation of insoluble dioxolanates consisting mainly of the complex "1,3-dioxolane-MgBr₂." Precipitation obtained by the Grignard reagent in 2-methyl-1,3-dioxolanes was earlier observed by Blomberg et al. [19], but this complex was not studied, and no attempt was made at interpreting this phenomenon. The specific structural features of the reaction under study and its selectivity with respect to the specific spatial isomers agree satisfactorily with the above diagram. The high reactability of the cis-isomer suggests that the plane of the transitory formation is oriented spatially at an angle to that of the dioxolane ring, since in a strictly planar junction of the rings there would be no spatial difference between the isomers in the transitory state. Such explanation is far from arbitrary if we consider that the free electron pairs of the oxygen are spatially oriented as to form close to tetrahedral angles with the valence bonds (the direction of the donor-acceptor bond in the oxygen-containing rings should protrude from the ring plane), due to hybridization of the oxygen electron orbitals tending toward sp³. It is obvious that increasing length of alkyl substituents will inversely affect the degree of steric selectivity of the reaction, due to the appearance of additional conformers caused by bends in the substituent chain.

The above ratios for the rates of cis- and trans-isomers of 2,4-dimethyl- and 3-propyl-4-methyl-1,3-dioxolanes confirm our conclusion.

EXPERIMENTAL

<u>Synthesis and Purification of Starter 1,3-Dioxolanes</u>. The dioxolanes (I)-(III) were obtained by reacting 1,2-propylene glycol with the corresponding aldehydes at a ratio 1:1 of the reagents in the presence of catalytic amounts of p-toluenesulfonic acid. The (III) obtained were transferred in a benzene medium, using the Dean-Stark separator; (I) and (II) were directly distilled from the reaction mixture during the process. After drying over potash, boiling for 2 h over metallic sodium and distilling over sodium, the following were obtained: (I), yield 56.8%, bp 80-82°C (716 mm); n_D^{20} 1.3980; d_4^{20} 0.9882; (II), yield 27%; bp 91°C (715 mm); n_D^{20} 1.3955; d_4^{20} 0.9272; (III), yield 47.3%; bp 140-141°C (717 mm); n_D^{20} 1.4112; d_4^{20} 0.9005.

2,4-Dimethyl-1,3-dioxolane (II) was also obtained according to the following technique: 1,2-propylene glycol was mixed with vinylbutyl ether at a 1:1 ratio in the presence of phosphoric acid, and the reaction mixture was distilled at atmospheric pressure. The distilled cyclic acetal was purified by rectification over metallic sodium. The yield of (II) was 60.0%.

Reaction of 2,4-Dimethyl-1,3-dioxolane (II) with the Grignard Reagent. A Grignard reagent was prepared from 2.4 g magnesium in 100 ml ether and added with 10.2 g of (II). After 30 min stirring, the ether was removed when the mixture started to assume a pasty consistency. The reaction mixture was heated at 80°C for 1 h, diluted with saturated aqueous NH₄Cl solution and after extraction, drying, and removal of the ether analyzed by GLCH (see Fig. 2b). Fractional distillation yielded 7.1 g (53.5%) (V); bp 41-41.5°C (3 mm); n_D^{20} 1.4179; d_4^{20} 0.8833. Found %: C 63.91, 64.10; H 12.21, 12.25; MR 37.71. C₇H₁₆O₂. Calculated %: C 63.59; H 12.20; MR 37.90.

From (III) we obtained under the same conditions a mixture whose composition (after evaporation of the ether) is shown on the chromatogram (see Fig. 3b). The hydroxyl ether (VI) was isolated at a 71.6% yield; bp 78-80.5°C (10 mm); n_D^{20} 1.4267; d_4^{20} 0.8816. Found %: C 67.50, 67.61; H 12.48, 12.51; MR 46.64. $C_9H_{20}O_2$. Calculated %: C 67.45; H 12.58; MR 46.20.

Interaction of 4-Methyl-1,3-dioxolane (I) with the Grignard Reagent. We heated 0.1 M (I) with 0.2 M ethylmagnesium bromide in 30 ml toluene at 108°C for 5 h (standard processing) and obtained 4.1 g (37.7%) of (IV); bp 59.5-60.5°C (20 mm); n_D^{20} 1.4171; d_4^{20} 0.8935. The chromatogram is shown in Fig. 1.

GLCH analysis was conducted on the LKHM-5 instrument with a detector for heat conductivity. The column was 4.2 m long and had a 6 mm diameter. The stationary phase was diheptylsebacinate, the carrier NaCl with a 0.25-0.5-mm grain size; helium was the gas carrier. We assigned peaks 1 and 2 to the specific configurations on the basis of chromatographic data under the following conditions: column of 5 m length, 6 mm diameter; stationary phase, squalane; carrier, chromosorb W, 45-60 mesh size.

Synthesis of Standard Hydroxy Ethers (X) and (XI). We obtained the hydroxy ether (X) from 2-methyl-1,3-dioxolane and ethylmagnesium bromide (ratio of reagents 1:2, benzene, 80°C, 3 h) with a 84.6% yield; bp 46-46.5°C (9 mm); n_D^{20} 1.4158; d_4^{20} 0.8999. Found %: C 61.38, 61.48; H 11.87, 12.26; MR 32.94. $C_6H_{14}O_2$. Calculated %: C 60.98; H 11.94; MR 33.25.

2,4-Dimethyl-2-ethyl-1,3-dioxolane, treated with the Grignard reagent under the same conditions gave the hydroxy ether (XI), at a 82.3% yield; bp 84-86°C (13 mm); n_D^{20} 1.4354; d_4^{20} 0.8923. Found %: C 68.92, 69.19; H 12.68, 12.87; MR 51.00. $C_{10}H_{22}O_2$. Calculated %: C 68.91; H 12.72; MR 51.84.

Obtention of Chloro-Ethers (VIII) and (IX). We heated 6.6 g (V) and 6 g SOCl₂ at 70°C in a pyridine medium for 3 h. The fluid was decanted, the precipitate washed with ether. After removal of the ether by fractional distillation under vacuum we obtained 2.0 g (75.2%) of (VIII); bp 40-41.5°C (10 mm); n_D^{20} 1.4170; d_4^{20} 0.9261.

The chloro-ether (IX) was obtained at a 63.3% yield; bp 73° C (11 mm); np²⁰ 1.4290.

Obtention and Analysis of the Complex Formed by 4-Methyl-1,3-dioxolane(1) with the Grignard Reagent. We prepared a25-ml ether solution of ethylmagnesium bromide containing 0.043 g-equiv. of the organomagnesium compound and added 2.2 g of (I). The precipitate which formed was filtered off at once, washed with ether and dried in the vacuum-desiccator. We obtained 5.9 g of a yellowish powder which decomposed at 106-158°C. The content in organomagnesium compounds was determined by acid titration: for 0.3241 and 0.2196 g of precipitate we used 4.8 and 3.3 ml 0.1 N HCl respectively which corresponds to 0.0015 g-equiv./g. Analysis of the ether filtrate showed that it contains 0.027 g-equiv. of organomagnesium compounds. Found %: C 20.51, 20.24; H 4.91, 4.88; Mg 9.29, 9.61; Br 45.35, 45.38.

The analytic data would correspond to the following composition of the complex: $[1.65 (I) \cdot MgBr_2 + (I) \cdot MgBr(C_2H_5)]$. Calculated %: C 21.6; H 3.74; Mg 9.12; Br 49.2. The content in organomagnesium compounds was 0.00143 g-equiv./g. The precipitate also contains a certain amount of solvates of the type: $O \cdot MgBr_2$, $(C_2H_5)_2O \cdot MgBr_2$, $(C_2H_5)_2O \cdot MgBr(C_2H_5)$ and others; they may be seen from G LCH identification of a sulfo-ether together with 4-methyl-1,3-dioxolane in the products derived from hydrolysis of the complex. The isolated complex may have the structure of a coordinated polymer.

CONCLUSIONS

1. The reaction between 4-methyl- and 2,4-dialkyl-1,3-dioxolanes and the Grignard reagent shows specific structural features, since only one of the possible hydroxyl ethers is formed.

2. IR spectroscopy and GLCH analysis were used to determine the structures of the hydroxy ethers; based on these findings, it was shown that the Grignard reagent splits the nonsymmetrically substituted dioxolanes under study at the O_1-C_2 bond.

3. The reaction is selective with respect to the spatial isomers of 2,4-dialkyl-1,3-dioxolanes (the cis-isomer reacts faster).

4. The reaction of 4-methyl-1,3-dioxolane with ethylmagnesium bromide was used as an example to show that insoluble solvates form at the first reaction stage; these consist mainly of a complex of cyclic acetal with magnesium bromide.

5. The findings agree with a mechanism involving cyclic migration of electrons in the six-membered ring formed by the complex "acetal-magnesium bromide" and magnesium diethyl.

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